REMARKS/ARGUMENTS

With this amendment, claims 1-5 and 17-19 are pending. Claim 4 is withdrawn; claims 6-16 are cancelled. New claims 17-19 are added. For convenience, the Examiner's rejections are addressed in the order presented in the November 24, 2004 Office Action.

I. Status of the claims

Claims 1 and 5 are amended to recite "an isolated SLIM nucleic acid molecule." Support for these amendments is found throughout the specification, for example, at page 16, lines 18-20. These amendments do not add new matter.

Claim 1 is amended to recite that a nucleic acid sequence having at least about 95% identity to a reference sequence. Support for this amendment is found throughout the specification, for example, at page 15, lines 9-10. This amendment does not add new matter.

New claims 17-19 are added and are directed to expression vectors that comprise SLIM nucleic acids, host cells that comprise the expression vectors, and methods of making SLIM proteins using the host cells and expression vectors. Support for these amendments is found throughout the specification, for example, at page 22, lines 13-36; and at page 23, lines 14 through page 24, line 15. These amendments do not add new matter.

II. Objections to the disclosure

The Office Action objected to figure numbering in certain figure legends. In order to expedite prosecution, the figure legends have been amended as indicated in the Office Action. The Office Action also objected to use of SLIM-DC in place of SLIM-ΔC. In order to expedite prosecution the specification has been amended as indicated in the Office Action. In view of the amendments to the specification, withdrawal of the objections to the disclosure is respectfully requested.

III. Rejections under 35 U.S.C. §101

Claims 1-3 and 5 are rejected under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. In order to expedite prosecution claims 1 and 5 are amended to recite an "isolated nucleic acid molecule". In view of this amendment, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §101.

IV. Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 1-3 and 5 are rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement. According to the Office Action, the specification lacks description of the claimed invention, such that a skilled artisan would recognize that Applicants had possession of the claimed invention at the time of filing. The claims are directed to nucleic acids that encode SLIM proteins. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

The Office Action alleges that the specification does not disclose nucleic acid molecules that comprise SEQ ID NO:1, or that comprise a nucleic acid that encodes SEQ ID NO:2, or that comprise a nucleic acid molecule with at least about 90% identity to SEQ ID NO:1. This allegation is incorrect. The specification provides both description and examples of nucleic acid molecules that comprise SEQ ID NO:1 or that comprise a nucleic acid sequence with at least about 95% identity (as is now claimed) to SEQ ID NO:1, or that comprise a nucleic acid that encodes SEQ ID NO:2.

SLIM proteins are defined as being encoded by SLIM nucleic acids. *See, e.g.*, specification at page 14, lines 13-15. The SLIM proteins can include other amino acid sequences that are encoded by nucleic acid molecules comprising SLIM nucleic acids, for example epitope or purification tags or fusions to reporter genes or fluorescent proteins. *See, e.g.*, specification at page 14, lines 8-11. At page 21, lines 11-32, the specification discloses chimeric molecules comprising a SLIM polypeptide fused to another, heterologous polypeptide or amino acid sequence. A number of tag polypeptides that can be encoded by the claimed nucleic acids molecules are disclosed: poly-his, poly-his-gly, flu HA, c-myc, Herpes Simplex virus glycoprotein D, FLAG, KT#, tubulin and the T7 gene 10 protein peptide. Nucleic acids that

comprise a SLIM nucleic acid and regulatory sequences, *i.e.*, expression vectors, are disclosed at page 22, lines 13-36. Retroviral vectors that comprise SLIM nucleic acids are also disclosed page 23, lines 30-34. Fusion and labeled SLIM nucleic acids and proteins are also disclosed at page 24, lines 17-31.

Examples of nucleic acids the comprise SLIM nucleic acids or their encoded amino acid sequences are found, *e.g.*, page 58, lines 1 and 2, which provides SLIM nucleic acids that encode a SLIM protein fused to a FLAG epitope. The encoded epitope-tagged SLIM proteins were used to inhibit CD69 induction in B and T cells. *See, e.g.*, Example 3, pages 60-61; Figures 3, 6 and legends. The encoded epitope-tagged SLIM proteins were used to investigate the function of specific domains of SLIM protein. *See, e.g.*, Example 4, page 62; Figure 4, 8, and legends. The encoded epitope-tagged SLIM proteins were used to investigate associate of SLIM protein with tyrosine phosphoproteins. *See, e.g.*, Example 5, page 63; Figure 5, 9, and legends. The encoded epitope-tagged SLIM proteins were also used to investigate the role of SLIM proteins in antigen-induced calcium mobilization. *See, e.g.*, Figure 7 and legend. Thus, the specification provides both description and examples of nucleic acid molecules that comprise SEQ ID NO:1 or that comprise a nucleic acid sequence with at least about 90% identity to SEQ ID NO:1, or that comprise a nucleic acid that encodes SEQ ID NO:2.

The Office Action also appears to allege that definitions of SLIM nucleic acid and SLIM protein are not included in the application. *See, e.g.*, Office Action at page 5, first full paragraph. This is not correct. SLIM proteins are defined in the specification at, *e.g.*, page 11, line 34 through page 12, line and page 12, lines 12-24. SLIM nucleic acid is defined at *e.g.*, page 15 line 12 through page 16, line 24. Based on these definitions, one of skill would believe that the inventors had possession of the claimed nucleic acids molecules.

The specification also appears to assert that the genus of SLIM nucleic acids and encoded proteins is not described in the specification. *See, e.g.*, Office Action at page 5, second full paragraph. However, as currently applied, the specification does comply with US patent law for description of a nucleic acid or amino acid sequence. The Guidelines for Examination of Patent Application Under 35 U.S.C. 112, ¶1, "Written Description" Requirement, ("The Guidelines for Written Description," Fed. Reg. 66, 1099 (2001)), address the description

adequate to show one of skill that the inventors were in possession of a claimed genus at the time of filing. An applicant may also show that an invention is complete by

> . . . disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. 66 Fed. Reg. 1099, 1106 (2001), citations omitted.

Furthermore, "description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *Id.*

Applicants provide structural and functional description of the claimed genus of nucleic acid molecules and encoded proteins required by the written description requirement. First, applicants provide exemplary sequences for the genus of SLIM nucleic acids and encoded proteins at SEQ ID NO:1 and 2. Applicants also provide instruction on how to identify nucleic acid sequences or amino acid sequences that have a specified % identity to the reference sequences at pages 12, line 12 through page 13, line 21 and at page 14, lines 12-19. Applicants also provide disclosure of structural domains within the SLIM protein that have particular functions. *See, e.g.*, specification at page 18, line18 through page 19, line 8. For example, amino acids 195-261 of SLIM appear to function in CBL binding. CBL binding to SLIM protein is disclosed in the specification, *e.g.*, at page 40, line 7 through page 41, line 2; and at page 62, line 38 through page 63, line 33; and Figures 5 and 9. The N-terminus of the SLIM protein has a myristolation domain that functions in membrane localization of the protein. The application discloses that mutation of the second glycine of the SLIM amino acid sequence blocks membrane localization. The disclosure also identifies an SH2 and SH3 sequences (*i.e.*, structures) in the SLIM protein at Figures 2A and 2B. Although the functions of those domains

were well known at the time of filing, they are also disclosed in the specification. SH2 domains bind to tyrosine phosphorylated partners; SH3 domains bind to proline rich sequences. This disclosure of the SLIM nucleic acid and amino acid sequences with the identification of a combination of specific structures, *e.g.*, CBL binding, myristolation, SH2, and SH3, and their functions allows the skilled artisan to understand that the inventors were in possession of the claimed invention at the time of filing.

Applicants direct the Examiner's attention to Example 14 of the Synopsis of Application of Written Description Guidelines which analyzes a claim directed to a protein having an amino acid sequence at least 95% identical to SEQ ID NO:3 and that has a specific activity. In these Guidelines, the Patent Office concluded that the claim was adequately described within the meaning of 35 U.S.C. §112, first paragraph. Therefore, on the basis of Written Description Guidelines issued by the USPTO, the claims meet the written description requirement.

In view of the above amendments and remarks, withdrawal of the rejection for alleged lack of written description is respectfully requested.

V. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 1-3 and 5 are rejected under 35 U.S.C. §112, first paragraph because the specification allegedly fails to comply with enablement requirement. In particular, the Office Action alleges that nucleic acid sequences comprising SEQ ID NO:1 or that encode proteins that comprise SEQ ID NO:2 are not enabled. In addition, the Office Action alleges that specification lacks guidance for the structure and function of the claimed nucleic acid genus and that this would allegedly result in undue experimentation for one of skill to make and use the invention. To the extent the rejections apply to the amended claims, Applicants respectfully traverse the rejection.

The Office Action alleges that those of skill in the art would be subject to undue experimentation in order to make and use the claimed nucleic acid sequences. First, Applicants submit that the disclosure teaches generally how to identify the claimed nucleic acids and how to assay for the encoded SLIM proteins with Cb1 binding activity. Second, claims reading on

inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. *See*, *In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971). In the present application, one of skill would know how to avoid inoperative embodiments and test for binding of the encoded SLIM proteins to Cb1 proteins. Moreover, the present application provides guidance in the form of assays to perform such tests.

As discussed above, the specification provides exemplary sequences for the genus of SLIM nucleic acids and encoded proteins at SEQ ID NO:1 and 2. Applicants also provide instruction on how to identify nucleic acid sequences or amino acid sequences that have a specified % identity to the reference sequences at pages 12, line 12 through page 13, line 21 and at page 14, lines 12-19. Based on this disclosure, one of skill would be able to identify SLIM nucleic acids within the scope of the claims, including nucleic acids that comprise SEQ ID NO:1 or related sequences. The specification provides both description and examples of nucleic acid molecules that comprise SEQ ID NO:1 or that comprise a nucleic acid sequence with at least about 95% identity (as is now claimed) to SEQ ID NO:1, or that comprise a nucleic acid that encodes SEQ ID NO:2. The encoded SLIM proteins can include other amino acid sequences that are encoded by nucleic acid molecules comprising SLIM nucleic acids, for example epitope or purification tags or fusions to reporter genes or fluorescent proteins. *See, e.g.*, specification at page 14, lines 8-11; page 21, lines 11-32; page 22, lines 13-36; page 23, lines 30-34; and page 24, lines 17-31. Examples of proteins that comprise SEQ ID NO:2 and the nucleic acids that encode them are disclosed in the specification as indicated in the discussion of the written description requirement above.

The Office Action also alleges that undue experimentation would be required to identify amino acid residues that are required to retain functional activity. Applicants respectfully traverse. Applicants have identified functional domains within the SLIM protein, including well understood domains such as a myristolation domain, an SH2 domain and an SH3 domain. Moreover, Applicants have provided assays for those of skill to determine binding of SLIM proteins to the Cb1 protein as required by the claims. Cb1 binding assays are found in the specification, *e.g.*, at page 40, line 7 through page 41, line 2; and at page 62, line 38 through page 63, line 33; and Figures 5 and 9, and include well-known and routinely utilized techniques, such

as immunoprecipitation and Western blotting. In addition, the use of these techniques can be facilitated with epitope tagged SLIM proteins, *i.e.*, proteins that comprise SEQ ID NO:2. The disclosed Cb1 binding assays can be used to identify operative and inoperative embodiments of the claimed nucleic acids sequences. Therefore, the specification and the knowledge of the art of routine techniques, such as immunoprecipitation and Western blotting, provide enablement for the claimed SLIM nucleic acid molecules.

In view of the above amendments and remarks, withdrawal of the rejection for alleged lack of enablement is respectfully requested.

VI. Rejections under 35 U.S.C. §112, second paragraph

Claims 1-3 and 5 are rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. First, claims 1-3 and 5 are rejected for use of the term "nucleic acid". In order to expedite prosecution, the claims are amended to recite "nucleic acid molecule", as suggested by the Office Action. Second, claim 3 is rejected for use of the term "further comprising". In order to expedite prosecution, claim 3 is amended to remove that term.

In view of the above amendments and remarks, withdrawal of the rejections under 35 U.S.C. §112, second paragraph is respectfully requested.

VII. Rejections under 35 U.S.C. §102

A. Introduction

Claims 1-3 and 5 are rejected under 35 U.S.C. §102 as allegedly anticipated in view of various references. To anticipate a claim, the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found...in a single prior art reference." *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Thus, in order to anticipate, the cited references must contain every element of the claims at issue and the cited references must be properly cited as prior art references. As discussed in detail below, the Office Action has incorrectly awarded the claims a filing date of January 10, 2002. The correct priority date is the filing date of the priority application, USSN 60/260,953, filed January 10, 2001. Thus, many of

the references were not properly cited as prior art. In addition, Applicants provide evidence that the priority application for cited reference US2004/0039163A1 (Burgess *et al.*) did not disclose all the elements of the claimed invention.

B. Disclosure of priority application 60/260,953

For the purpose of the art rejections, the Office Action has deemed the filing date of claims 1-3 and 5 to be January 10, 2002. The Office Action alleges that the earliest filed priority application, USSN 60/260,953, (the '953 application), filed January 10, 2001, does not disclose a nucleic acid sequence having at least about 90% identity to SEQ ID NO:1 as is claimed. According to the Office Action, the '953 application discloses only 90% homology between reference and claimed sequences. These assertions are incorrect.

The '953 application provides ample disclosure of identity with respect to reference sequences. Homology is defined generally at page 25, lines 10-11 of the '953 application. "Homology in this context means sequence similarity or identity, with identity being preferred." The '953 application also teaches how to determine identity of an amino acid sequence or a nucleic acid sequence using an appropriate BLAST algorithm. See, *e.g.*, '953 application at page 26, line 9 through page 27, line 6. Using the definition of homology found in the '953 application the cited passage at page 29, last paragraph provides support for a nucleic acid having at least about 95% identity to SEQ ID NO:1. Thus, the '953 application provides disclosure of a nucleic acid having at least about 95% identity to SEQ ID NO:1 as is claimed and therefore, the filing date of the '953 application, January 10, 2001, is the correct priority date for the claims.

C. Alleged anticipation by Holland et al.

Claims 1-3 and 5 are rejected under 35 U.S.C. §102(a) as allegedly anticipated by Holland *et al.* J. Exp. Med. 194:1263-1276 (2001). Holland *et al.* was published on November 5, 2001, well after the January 10, 2001 filing date of the priority '953 application. As such, Holland *et al.* is not properly cited as prior art against the claimed invention.

D. Alleged anticipation by GenEmbl Accession No. AF326353

Claims 1-3 and 5 are rejected under 35 U.S.C. §102(a) as allegedly anticipated by GenEmbl Accession No. AF326353. Applicants submit as Exhibit A, a revision history for GenEmbl Accession No. AF326353, which indicates that the sequence was first seen at NCBI on November 8, 2001, well after the January 10, 2001 filing date of the priority '953 application. As such, GenEmbl Accession No. AF326353 is not properly cited as prior art against the claimed invention.

E. Alleged anticipation by US2004/0039163A1

Claims 1-3 and 5 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by US2004/0039163A1 to Burgess *et al.* US2004/0039163A1 claims priority to a provisional application, USSN 60/228,191 (the '191 application), filed on August 25, 2000. Applicants respectfully traverse the rejection, and herein provide evidence in the form of sequence alignments (Exhibits B and C) that the claimed subject matter was not disclosed in the '191 application.

The Office Action alleges that Burgess *et al.* discloses a nucleic acid molecule SEQ ID NO:74 that encodes a protein of 261 amino acid residues that is 100% identical to SEQ ID NO:2. This allegation is incorrect. First, Applicants assert that the claimed reference sequences, SEQ ID NO:1 and SEQ ID NO:2 were disclosed in our priority '953 application, filed on January 10, 2001. For analysis under 35 U.S.C. §102(e), SEQ ID NOs:1 and 2 are properly compared to the sequences found in the '191 application, and not the sequences in the later published Burgess *et al.* reference. SEQ ID NO:74 of Burgess *et al.* is also referred to as 87919652. See, Burgess *et al.* page 91, paragraph 273, line 2. The '191 application discloses a nucleic acid and an amino acid sequence both referred to as 87919652. See, *e.g.*, '191 application at page 109. Applicants submit as Exhibit B, a sequence alignment between the 87919652 amino acid sequence of the '191 application and SEQ ID NO:2. The sequences are not identical and differ by one amino acid. Applicants also submit as Exhibit C, a sequence alignment between the 87919652 nucleic acid sequence of the '191 application and SEQ ID NO:1. The nucleic acid sequences share only 43.3% identity. Applicants also assert that, as

written, the 87919652 nucleic acid sequence of the '191 application does not encode a SLIM protein. Therefore, as the priority application for the cited Burgess *et al.* publication, the '191 application, does not disclose all the elements of the claims, it cannot anticipate the claimed invention.

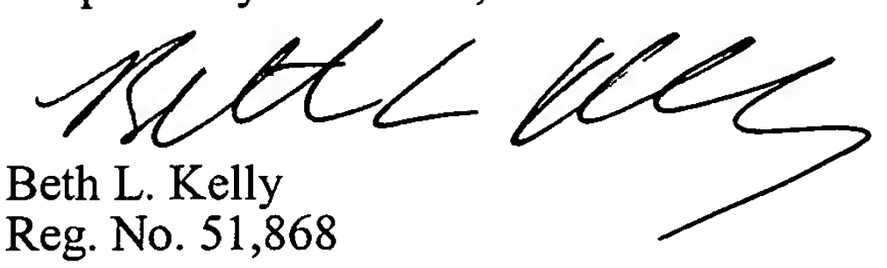
In view of the above arguments, Applicants respectfully request that the rejections under 35 U.S.C. §102 be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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